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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,882	11/16/2000	C. Alexander Turner JR.	LEX-0091-USA	5490

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/714,882	Applicant(s) TURNER ET AL.	
	Examiner Eileen O'Hara	Art Unit 1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 May 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *07 March 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-8*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *notice of references cited*

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because: Applicants argue that the final action disagrees with Applicants' logical assertion, based on the evidence, that the sequences of the present invention encode novel members of the Notch ligand family, however, to the contrary, it was not asserted in the final action that the sequences of the invention are not members of the Notch ligand family (page 3 of action). Due to the high level of similarity (46% similar to SEL-1), the sequences of the instant invention are probably members of the Notch ligand family, but it is not predictable that they have the same activity as SEL-1, since they are 54% divergent, and it is Applicants' assertion that the utility of Notch ligands is well established and known to those of skill in the art that is at issue. Applicants' arguments on pages 2-3 of the response that the Yan paper et al. cites only one example of two isoforms, and that the two amino acid change results in binding to two different receptors that are related, and that the EDA-A2 receptor was correctly identified as a member of the tumor necrosis receptor superfamily based solely on sequence similarity is hardly indicative of a high level of uncertainty in assigning function based on sequence or family membership, and thus does not support the alleged lack of utility, have been fully considered but are not deemed persuasive. Although the EDA-A1 and EDA-A2 receptors of Yan et al. are related, they are distinct. On page 526, 1st column, Yan et al. states "Regardless, the distinctive temporal and spatial expression of EDA-A1 and EDA-A2 suggest that they may have distinct roles in development of the hair follicle." Therefore, the ligands for these receptors would also have distinct physiological roles, though they may both bind to related receptors and be involved in hair follicle morphogenesis. Applicants' argue that a number of older articles which are said to support the proposition that function cannot be predicted based on structural information do not refer to Notch ligands. It is not relevant that the articles don't refer to Notch ligands; these articles were cited to demonstrate that in different types of protein families, even it there are structural similarities between proteins, the function of one cannot be reliably predicted from that of another. Applicants' arguments that the Ji reference suggests that homology with members of a G-protein coupled receptor is indicative that the particular sequence is in fact a member of that family and supports Applicants' assertion that a structure function relationship is well-established have been fully considered but are not deemed persuasive. It is not disputed that homology with members of a family is indicative that the particular sequence is a member of that family; a structure-family membership may be well-established, but not a structure-function relationship. For example, members of the G-protein coupled receptor family may have similar structural features and all may couple to G proteins to facilitate signal transduction, however the properties, functions and uses of such GPCRs is widely variable, and they do not have the same uses and activities. Applicants' arguments that there is no statutory requirement for the disclosure of a specific example (In re Gay) and that the Applicants' assertion of the stated utility is legally sufficient and should control the utility analysis unless the Examiner meets the burden of establishing the lack of utility by making evidence of record that conclusively refutes the Applicants' asserted utility have been fully considered but are not deemed persuasive. In some instances disclosure of a specific example may not be necessary. For example, a novel DNA ligase discovered that is 95% identical to a known DNA ligase would not necessarily require an example to provide utility, because ligases are highly conserved, the extent of homology is extremely high, and DNA ligases all have the same activities, that of ligating DNA. That situation is very different from the present instance, in which a much lower level of homology is disclosed, and there is no common function. There are different Notch family ligands that bind to different Notch receptors that are expressed in different cell types and have different activities, and the Notch signaling pathways are very complicated (see attached articles, Baron et al., Molecular Membrane Biology, 2002, Vol. 19, pages 27-38, Portin, P., Hereditas, 2002, Vol. 136, No. 2, pages 89-96 and Baron et al., Seminars in Cell and Developmental Biology, April, 2003, Vol. 12, No. 2, pages 113-119). Applicants arguments on pages 3-4 that absent a change in law as enacted by Congress and signed by the President, it is improper for the Examiner to hold Applicants' invention to a different legal standard of patentability, and that Applicants' invention is more enabled that inventions in previous cited U.S. patents, have been fully considered but are not deemed persuasive. The Examiner has no authority to comment on the validity of issued U.S. patents or the current guidelines, and has examined the instant application Applicant as determined by the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001. Applicants' arguments on pages 4-5 of the response that the use of the presently claimed polymorphic polynucleotides on DNA chips have a specific utility, as they have been identified to contain several coding region single nucleotide polymorphisms and thus increase their utility in DNA gene chip analysis, and that as the claimed sequences provide a specific marker of the human genome, such markers are targets for discovering drugs that are associated with human disease and would be useful for assessing gene expression, have been fully considered but are not deemed persuasive. Regarding the merit of the argument, any new polynucleotide can be used in a microarray, and thus this asserted utility is not specific. Also, the disclosure that the NHP proteins of the instant invention are structurally related to SEL-1 does not render the asserted utility specific, since the specification does not establish they are expressed in any diseased tissues in any way that is different from the way it is expressed in healthy forms of the same tissues. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify diseases states which correlate with altered levels or forms of the claimed polynucleotides. Therefore, this asserted utility is also not substantial. Applicants also assert that further evidence of the utility of the presently claimed polynucleotide is the specific utility in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions, and in localizing the specific region of the human chromosome, a utility which is not shared by virtually any other nucleic acid sequences. Applicants also submit that the practical scientific value of expressed, spliced and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts, and the sequence provides a unique and specific resource for mapping the genome, and provides in Exhibit D the identification of functionally active intron/exon splice junctions, identifying that the protein is encoded by 20 exons. Applicants' arguments have been fully considered but are not deemed persuasive. While identifying the region a gene is located on in a chromosome and identifying the introns and exons are scientifically interesting, it is not clear to the examiner why mere information on structure or location of a gene on the chromosome would be a patentable utility. For these reasons and those discussed in the previous office actions, the rejections are maintained.